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# THE QUALITATIVE SEPARATION AND IDENTIFICATION OF SOME OXYMETHYLANTHRAQUINONES.

By E. Monroe Bailey.

The color principles in medicinal plants are not, as a rule at least, their so-called "active principles,"—that is, the constituents upon which the therapeutic value of the plants depends,—but they are so intimately associated with these constituents that a knowledge of their behavior is of service both in the assay of crude drugs and in the examination of medicinal preparations.

The common cathartic drugs, senna, rhubarb, aloes, and the various species of buckthorn, are characterized by a group of color principles known as oxymethylanthraquinones. These compounds are derivatives of the fundamental substance anthracene, $C_{14}H_{10}$, or, more directly, of its diketone, anthraquinone, $C_{14}H_8O_2$. From these two substances a large group of vegetable colors is derived.[1] Although the oxymethylanthraquinones are not confined to the cathartic drugs, their presence will usually indicate a more or less restricted group of plants of medicinal value. None of the above-named drugs is characterized by a single anthraquinone derivative, but, rather, each contains a mixture of several of them, so that the identification of any particular oxymethylanthraquinone fails of the diagnostic value it would otherwise have. Mossler,[2] however, has differentiated between senna, rhubarb, and cascara on the basis of the oxymethylanthraquinone crystals obtained by recrystallization from hot acetic acid.

The Borntträger reaction[3] is given by all the natural oxymethyl-

[1] Czapek, "Biochemie der Pflanzen II," p. 528.
[2] Through *Analyst* **38**, 321 (1913).
[3] *Zeit. anal. Chem.* (1880), p. 165.

anthraquinones.[4] This test depends upon the production of a red color in the aqueous liquid when an ethereal solution of oxymethylanthraquinones is washed with dilute alkali. This cannot be regarded as a specific test, since other colors, both natural and synthetic, behave similarly. The writer's experience with such conditions led to the outline of a procedure[5] to distinguish chrysophanic acid (dioxymethylanthraquinone) in the presence of phenolphthalein, næmatoxylin, and curcumin.[6] After hæmatoxylin and curcumin have been eliminated, chrysophanic acid is distinguished from phenolphthalein by reducing both substances with zinc dust and dilute sodium hydroxide, whereupon chrysophanic acid is reduced to its anthranol, which is readily reoxidized by exposure to air, dilution with water, or, best, by the addition of a few drops of hydrogen peroxide, a pink-red color resulting. Phthalin is not sensitive to this method of oxidization, and remains colorless. This procedure constitutes a much more specific test for oxymethylanthraquinones than the Bornträger reaction. Warren[7] has applied it to mixtures of phenolphthalein with senna, cascara, and aloes, and obtained satisfactory results. In case of aloes he found that upon reoxidization the red color was slow to appear, and was somewhat masked by yellow coloring matter. This point will be referred to later. Warren has also perfected a method to effect the separation of phenolphthalein in presence of oxymethylanthraquinones which depends upon the removal of phenolphthalein as its tetraiodo compound, leaving the anthraquinone derivatives to be tested for in the usual way.

It was originally our hope to find some color reaction which would serve to differentiate between the cathartic drugs already mentioned. While experiments have thus far fallen short of success in this respect, they have, nevertheless, led to some interesting differences among the oxymethylanthraquinones themselves, more especially between the dioxymethyl and trioxymethyl derivatives, chrysophanic acid and emodin respectively.

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[4] Tschirch und Pederson, *Arch. Pharm.*, **236**, p. 205 (1898).

[5] Bailey, *J. Ind. Eng. Chem.*, **6**, 4, 320.

[6] Of the two last-named substances, hæmatoxylin belongs to a group of colors distinct from the anthracene derivatives, viz., the flavon group, while the constitution of curcumin shows it to be closely allied to the flavon derivatives. Czapek, "Biochemie der Pflanzen II," pp. 523 and 527.

[7] Am. Jour. Pharm., **86**, 10, 444–49 (1914).

To obtain the mixed color principles, hot extraction with benzol was employed, as recommended by De la Rue and Müller [8] in their work on rhubarb. Twenty-five Cc. of fluidextract of the various drugs examined were evaporated to remove alcohol, diluted with 25 Cc. of water, treated with an excess of normal lead acetate, and filtered through paper pulp on a Büchner funnel by the aid of suction. The lead precipitate, together with the paper pulp, was transferred to a beaker and digested for one hour with 10 per cent. sulphuric acid in a boiling water bath. The solution was filtered and the filtrate extracted, while still hot, with hot benzol. In the case of powdered drugs, three grammes of material were boiled with alcoholic potassium hydroxide under a reflux condenser for one hour. The solution was then evaporated to remove alcohol, diluted with 50 Cc. of water, acidified with dilute sulphuric acid, and extracted directly with hot benzol.

By washing the benzol solution first with 5 per cent. sodium carbonate solution and then with 5 per cent. sodium hydroxide, emodin and chrysophanic acid can be separated. The separation can be made quite sharp if one bears in mind that emodin is very readily soluble in sodium carbonate, and that chrysophanic acid is slightly soluble also. Two or three washings of the benzol solution with sodium carbonate are usually sufficient to remove emodin, and the aqueous solution is of deep red color. As the benzol is further washed with this reagent, the washings become pink-colored, due to the slight solubility of chrysophanic acid. Treatment with sodium carbonate, then, should be discontinued when the washings become pink. The chrysophanic acid can be readily removed by one or two washings with sodium hydroxide.

In a few preliminary experiments it was found that an initial treatment of the benzol solution with 5 per cent. ammonium carbonate removed a considerable amount of coloring matter which did not subsequently behave like either emodin or chrysophanic acid, but did, in most cases, give the test for oxymethylanthraquinones. On account of this fact, and since chrysophanic acid is practically insoluble in dilute ammonium carbonate, and emodin but slightly soluble, the addition of ammonium carbonate to the series of reagents for the fractional washing of the benzol extract suggested itself.

The procedure adopted, then, was to wash the benzol solution

[8] *Jour. Chem. Soc.* 10, 298.

in a separatory funnel, first with 25 Cc. portions of 5 per cent. ammonium carbonate until the washings were colorless or but faintly colored; then with similar portions of 5 per cent. sodium carbonate until the washings became pink colored; and, finally, with 5 per cent. sodium hydroxide, thus removing unidentified anthraquinone derivatives, emodin, and chrysophanic acid in the order named. The three aqueous solutions were then separately acidified and shaken out with ether, and the ether residues examined directly or after recrystallization from alcohol.

The differentiation of the several residues was made chiefly on the basis of their melting-points and color reactions. After testing the residues with various reagents for distinctive color reactions, it was found that the most striking differentiation was obtained by treating with concentrated sulphuric acid, concentrated nitric acid, and water successively in the following manner:

To the residue in a white porcelain capsule were added 4 to 5 drops of concentrated sulphuric acid, then 1 to 2 drops of concentrated nitric acid, and, finally, about 1 Cc. of water.[9] The initial color with sulphuric acid and the behavior on dilution with water constitute the characteristics of the test. The residue from a few drops of an ethereal solution of the color in question is sufficient for the test.

### Chrysarobin.

The procedure just described was first applied to commercial "chrysophanic acid." Since this substance is largely chrysarobin, about 3 grammes of the powder were dissolved in 100 Cc. of dilute (10 per cent.) sodium hydroxide and oxidized by passing air through the solution for one hour. The solution was then filtered, the filtrate acidified with dilute sulphuric acid, and a hot extraction made with benzol.

*Ammonium and Sodium Carbonate Fractions.*—A little color was removed by each of these reagents, but the fractions were not further examined.

*Sodium Hydroxide Fraction.*—The remaining color was removed completely from the benzol in one washing. The color was passed into ether and the ether evaporated at a gentle heat. The residue was amorphous; golden yellow in color; soluble in hot, but difficultly

[9] These reagents are the same as used by Cripps and Dymond in their test for aloes.—*Ber. Chem. Ges.*, **18**, 200 (1885).

soluble in cold, absolute alcohol; soluble in concentrated sulphuric acid with an orange-red color. The melting-point (r. h.) was not sharp, gradual liquefaction taking place between 160° and 165°. The behavior of the residue by the color test already described may be represented as follows:

Residue + $H_2SO_4$ = orange red; + $HNO_3$ = yellow; + $H_2O$ = yellow solution and flocculent precipitate.

The flocculent precipitate is chrysophanic acid unchanged.[10] Too much nitric acid prevents its formation.

### Buckthorn (Rhamnus Frangula).

As a source of emodin fluidextract of buckthorn was used. About 25 Cc. of this material were extracted with benzol as already described.

*Ammonium Carbonate Fraction.*—A little color was removed by this reagent. It was not further examined.

*Sodium Carbonate Fraction.*—Practically all the color was removed from the benzol at this point in two or three washings. The color was passed into ether and the ethereal solution evaporated. The residue was orange red in color; soluble in cold absolute alcohol; soluble in concentrated sulphuric acid with a decided pink color. The melting-point (r. h.) was not sharp; liquefaction extended over a range of about 5° and was complete at 240°.

The behavior of emodin by the color test as applied to chrysophanic acid is shown thus:

Residue + $H_2SO_4$ = intense pink; + $HNO_3$ = yellow; + $H_2O$ = pink solution.

*Sodium Hydroxide Fraction.*—The slight amount of color left in the benzol extract was removed at once by this reagent. The fraction was not further examined.

### Rhubarb.

The experimental material used was a fluidextract.

*Ammonium Carbonate Fraction.*—The first two or three washings of the benzol extract were orange-colored, after which practically no more color was removed. The color was passed into ether, but the residue was small, and only the general test for oxymethyl-

[10] Czapek, "Biochemie der Pflanzen II," p. 529.

anthraquinones was applied, which was positive. Whether this substance is rhein, tetroxymethylanthraquinone,[11] we are not prepared to say.

*Sodium Carbonate Fraction.*—Five or six washings with sodium carbonate were made. The alkaline solution was deep red. After this the washings became pink-colored, and the treatment was discontinued. The color was passed into ether and the ether evaporated. The residue was orange red and showed a tendency to form needle-like crystals. The melting-point was not sharp, but the substance was distinctly liquid at 249°. By the color test the reactions were like those found for emodin as derived from buckthorn.

*Sodium Hydroxide Fraction.*—Two washings completely removed the remaining color of the benzol extract. The ether residue obtained from this fraction was golden yellow in color and melted quite sharply at 189° to 190°. By the color test the reactions were like those observed for chrysophanic acid as derived from chrysarobin.

SENNA.

In the work with senna fluidextracts were used.

*Ammonium Carbonate Fraction.*—This reagent removed a large amount of color from the benzol in the first four washings, which were deep orange in color. Subsequent washings were faint pink, a slight amount of color being removed indefinitely. The color in the first four washings was passed into ether and the ether evaporated. The residue was evidently not a homogeneous substance. A portion of it went into solution readily in cold absolute alcohol, but the remainder dissolved only by the aid of heat. A difference in solubility was shown also with ether, and a separation was made into (*a*) ether-soluble and (*b*) ether-insoluble portions.

The ether-soluble portion (*a*) gave the general test for oxymethylanthraquinones. By the color test reactions not hitherto observed were obtained.

Residue + $H_2SO_4$ = purple or violet; + $HNO_3$ = yellow; + $H_2O$ = yellow solution.

No melting-point was obtained.

The ether-insoluble portion (*b*), on applying the general test for oxymethylanthraquinones, gave a purple-red solution on addition

[11] O. Hesse, *Proc. Am. Pharm. Assoc.* (1896), p. 549.

of soda, and the color was not discharged by boiling with zinc dust, but rather intensified. The hot solution was filtered, and the filtrate was of a brilliant deep red color. This color faded slowly, and the process was hastened by the addition of $H_2O_2$. After some minutes the solution became water-white, and a light-colored or white precipitate separated. At somewhat above 200° the material sublimed. No liquefaction had taken place at 290°, but a copious yellow sublimate had collected in the upper part of the capillary tube. This behavior is strikingly like that of anthraquinone itself.[12]

*Sodium Carbonate Fraction.*—A considerable amount of color was removed from the benzol by this reagent. When passed into ether and evaporated, the residue was orange red in color, but not crystalline. The melting-point was not sharp, but liquefaction was distinct at about 230°. The color test gave the reactions observed for emodin as derived from buckthorn and rhubarb.

*Sodium Hydroxide Fraction.*—The ether residue from this fraction was golden yellow in color. It fused at 185° to 190°, and was distinctly liquid at about 200°. By the color test reactions were obtained corresponding to those of chrysophanic acid as derived from chrysarobin and rhubarb.

## Aloes.

The experimental material consisted of Socotrine and Barbadoes varieties in powder form and a commercial fluidextract.

*Ammonium Carbonate Fraction.*—A considerable amount of color was removed from benzol, the washings being orange-colored. The ether residue was white or pale yellow, and not crystalline. The general test for oxymethylanthraquinones was positive, but faint and unsatisfactory, some foreign coloring matter evidently interfering. It is to this fraction that the difficulty noted by Warren,[13] on applying the test to aloes, is due. By the color test the following reactions were obtained:

Residue + $H_2SO_4$ = purple; + $HNO_3$ = yellow; + $H_2O$ = yellow solution.

This behavior corresponds to that obtained for the unidentified oxymethylanthraquinone derived in the corresponding fraction from senna.

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[12] Mulliken, vol. 1, p. 211; also p. 216, test 1011.

[13] Am. Jour. Pharm., **86**, 10, 444 (1914).

*Sodium Carbonate Fraction.*—The amount of color removed at this point was small. The general test for oxymethylanthraquinones was positive and characteristic. The color test gave reactions as follows:

Residue + $H_2SO_4$ = red, brownish; + $HNO_3$ = yellow; + $H_2O$ = yellow solution.

The intense pink color with sulphuric acid characteristic of this fraction in the cases of buckthorn, rhubarb, and senna was lacking. This peculiarity was encountered with both varieties of aloes and also with the fluidextract.

*Sodium Hydroxide Fraction.*—The greater part of the color in the benzol was removed at this point, and a copious ether residue was obtained. It was of the characteristic golden-yellow color; gave the general test for oxymethylanthraquinones, and by the color test, the characteristic behavior observed for chrysophanic acid as obtained from other sources in previous experiments. In case of Socotrine aloes the residue fused at 185° and liquefied at 189° to 192°. With Barbadoes aloes fusion took place at above 180°, with liquefaction at about 198°.

## Discussion.

The melting-points of chrysophanic acid as obtained from different drugs shows considerable variation. It is obviously not a pure product, the nature of the impurity depending upon the source from which it is derived. The melting-points for this substance recorded in the literature show also wide variations, figures from 162° to 191° being given.[14]

The melting-points obtained for emodin are in closer agreement among themselves, and in reasonable accord with those given in the literature, about 250°. Tschirch and Oesterle [15] find for alo-emodin a melting-point of 216°.

For the purposes of this investigation, however, melting-points have been regarded rather as broadly differentiating between the substances separated than as precise observations intending to indicate states of purity.

The procedure followed in the experiments described furnishes

[14] See Allen, "Commer. Organ. Anal.," 4th ed., vol. 5, p. 227. Beilstein, "Handb. d. Organ. Chem.," vol. 3, p. 452. Mulliken, "The Identification of Pure Organic Compounds," vol. 1, p. 208.

[15] *Ber. d. Pharm. Ges.*, 8, 174.

a satisfactory qualitative separation of the chief color principles in the drugs examined, and it is also believed that the separation can, within reasonable limits, be made quantitative.

The reaction utilized to identify chrysophanic acid in the presence of phenolphthalein [16] serves also as a test for oxymethylanthraquinones generally, and is much more specific for this group than the Bornträger reaction.

By the color test described emodin and chrysophanic acid give characteristic reactions. The distinguishing features are that emodin gives an intense pink color immediately on addition of concentrated sulphuric acid, and a pink solution, or one with a decided pink tinge, on final dilution with water; chrysophanic acid gives an orange-red color with sulphuric acid, and, on final dilution, gives a yellow solution and a yellow precipitate. The sodium carbonate soluble color fraction derived from aloes is an exception to the behavior of emodin as derived from buckthorn, rhubarb, and senna. The unidentified oxymethylanthraquinone, or mixture, obtained in the ammonium carbonate fraction is characterized by an intense purple or violet color with concentrated sulphuric acid. These reactions may be summarized as follows:

Emodin, as derived from buckthorn, rhubarb, and senna:

With conc. $H_2SO_4$ = pink; + $HNO_3$ = yellow; + $H_2O$ = pink solution.

As derived from aloes (sodium carbonate soluble):

With conc. $H_2SO_4$ = red, brownish; + $HNO_3$ = yellow; + $H_2O$ = yellow solution.

Chrysophanic acid, as derived from all sources:

With conc. $H_2SO_4$ = orange red; + $HNO_3$ = yellow; + $H_2O$ = yellow solution and precipitate.

Unidentified oxymethylanthraquinones (ammonium carbonate soluble):

With conc. $H_2SO_4$ = purple or violet; + $HNO_3$ = yellow; + $H_2O$ = yellow solution.

A relatively large amount of chrysophanic acid was present in the aloes examined. The color removed by sodium hydroxide was greatly in excess of that removed by sodium carbonate.

[16] *J. Ind. Eng. Chem.*, 6, 4, 320.

The nature of the sodium carbonate fraction in the case of aloes, and that of the ammonium carbonate fraction in all cases are among the interesting points suggested by the experience herein described, to which we hope to give further attention.

Analytical Laboratory,
Connecticut Agriculture Experiment Station,
New Haven, Conn.

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## STANDARDIZATION OF SODIUM THIOSULPHATE VOLUMETRIC SOLUTION.[1]

By Joseph L. Mayer.

A reference to page 563 of the U. S. P. will show that the official method of standardizing sodium thiosulphate V. S. is to employ a decinormal solution of potassium dichromate, proceeding as follows:

"To a solution of about 1 Gm. of potassium iodide (Potassii Iodidum, U. S. P.) in 10 Cc. of diluted sulphuric acid contained in a flask of about 500 Cc. capacity, add slowly, from a burette, 20 Cc. of tenth-normal potassium dichromate V. S., shaking after each addition. Place a watch-glass on the mouth of the flask and allow it to stand for five minutes, then dilute the solution with about 250 Cc. of distilled water, add some starch T. S., and then, from a burette, the trial solution of sodium thiosulphate, in small portions at a time, shaking after each addition, and, toward the end of the operation, reducing the flow to drops, until the blue color of the mixture changes to a light green; note the number of cubic centimetres of the trial sodium thiosulphate solution consumed. Then dilute the sodium thiosulphate solution so that equal volumes of it and the tenth-normal potassium dichromate V. S. will exactly correspond to each other under the above conditions at 25° C. (77° F.)."

On page 549 of the U. S. P. volumetric iodine solution is directed to be made by the following:

"Tenth-normal iodine V. S. may be prepared according to either of the following methods:

"1. Dissolve 12.59 Gm. of pure iodine (see below) in a solution of 18 Gm. of potassium iodide in 300 Cc. of water. Then add sufficient water to make the solution measure, at 25° C. (77° F.),

[1] Read before the Kings County Pharmaceutical Society, March 9, 1915.

exactly 1000 Cc. Unless freshly prepared, its strength should always be determined anew at the time it is used. Transfer the solution to glass-stoppered vials.

" Preparation of Pure Iodine.—Heat powdered iodine (Iodum, U. S. P.) in a porcelain dish placed over a bath of boiling water for twenty minutes, and stir it constantly with a glass rod, so that adhering moisture, cyanogen iodide, and most of the iodine bromide and iodine chloride, if present, may be vaporized. Then transfer the iodine to a porcelain or other non-metallic mortar, and triturate it with about 5 per cent. of its weight of dry potassium iodide, so as to decompose any remaining iodine bromide and iodine chloride. Then return the mass to the dish, cover it with a glass funnel, and heat the dish carefully on a sand-bath. Detach the sublimed, pure iodine, and, after pulverizing and drying for twenty-four hours over calcium chloride, keep it in well-stoppered bottles, in a cool place."

Since N/10 iodine is the exact equivalent of N/10 $Na_2S_2O_3$, the U. S. P., on page 550, gives as an alternative method of preparing the N/10 iodine the following:

" Dissolve about 14 Gm. of iodine (Iodum, U. S. P.) in a solution of 18 Gm. of potassium iodide (Potassii Iodidum, U. S. P.) in about 300 Cc. of water, diluting finally to 1000 Cc. Of this solution (which is too concentrated), carefully measure from a burette 10 Cc. into a flask, then add gradually and cautiously, from a burette, tenth-normal sodium thiosulphate V. S. (shaking constantly) until the color of the solution is discharged. Note the number of cubic centimetres of the sodium thiosulphate V. S. consumed, and then dilute the iodine solution so that any known volume of the latter will require for decolorization exactly the same volume of the tenth-normal sodium thiosulphate V. S."

This indicated to me that the factor for $Na_2S_2O_3$ V. S., standardized by either potassium dichromate or resublimed iodine, would be the same, and to determine whether such was actually the case the following work was undertaken. A N/10 $K_2Cr_2O_7$ V. S. was made up by the following method on page 551 of the U. S. P., employing Kahlbaum's salt:

" Dissolve 4.8713 Gm. of pure potassium dichromate, which has been pulverized and dried at 120° C. (248° F.) (see Reagent No. 85), in sufficient water to measure, at 25° C. (77° F.), exactly 1000 Cc."

The $Na_2S_3O_3$ V. S. standardized against this had the factor recorded in tabulation below.

Another lot of N/10 $K_2Cr_2O_7$ made up by the same method, using Baker's salt, the same $Na_2S_2O_3$ V. S., had the factor noted below.

Small amounts of iodine prepared as directed under V. S. iodine were weighed off and after solution in water with the aid of KI employed to standardize the $Na_2S_2O_3$ solution; the factor is recorded below.

Iodine prepared as directed by the U. S. P. under V. S. Iodine was mixed with KI placed in a small porcelain crucible, heated on a sand-bath until copious evolution of iodine fumes, when one of a set of watch-glasses with ground edges, which were tared with a clip, was slipped over the top of the crucible until a sufficient amount of iodine had sublimed, when, after cooling, the watch-glasses, clip, and iodine were weighed again, the increase being iodine. The watch-glasses and iodine without clip were then put into a few cubic centimetres KI solution, and when the iodine was dissolved the $Na_2S_2O_3$ V. S. was run in until the reaction was complete. The factor for the $Na_2S_2O_3$ solution is noted below.

Factor employing Kahlbaum's chemical—1 Cc. = 0.011342 gramme iodine; 1 Cc. = 0.9009 Cc. N/10 $Na_2S_2O_3$ V. S.

Baker's chemical—1 Cc. = 0.011362 gramme iodine; 1 Cc. = 0.9025 Cc. N/10 $Na_2S_2O_3$ V. S.

Iodine resublimed on funnel—1 Cc. = 0.011539 gramme iodine; 1 Cc. = 0.91652 Cc. N/10 $Na_2S_2O_3$ V. S.

Iodine resublimed on watch-glass—1 Cc. = 0.011533 gramme iodine; 1 Cc. = 0.91604 Cc. N/10 $Na_2S_2O_3$ V. S.

These results indicate that the use of resublimed iodine gives higher and probably more accurate results than the potassium dichromate method.

I am fully aware of the fact that the potassium dichromate used for standardization is usually directed to be checked against pure iron, as is evidenced by the following citation from page 136, U. S. Department of Agriculture, Division of Chemistry, Bulletin 107, revised, under the determination of the iodine number of fats and oils:

> "Decinormal Potassium Bichromate.—Dissolve 4.9083 grammes of chemically pure potassium bichromate in distilled water and make the volume up to 1 litre at the temperature at which the titrations are to be made. The bichromate solution should be checked against pure iron";

but, of course, this requires another determination and further complicates the standardization of the $Na_2S_2O_3$ V. S.

In view of the close duplicates obtained by the use of resublimed iodine and simplicity of employing the watch-glasses and clip method, I would suggest this as the most satisfactory means of accurately standardizing $Na_2S_2O_3$ V. S.

The sodium thiosulphate solution was made by taking 4 litres of distilled water, boiling until all air and $CO_2$ were expelled, placing in a large amber-colored bottle and, when cool, dissolving about 100 grammes of C. P. sodium thiosulphate in the liquid.

The bottle was set away in a dark place until ready for use (in about six weeks). When a syphon tube with pinch cock was inserted and a layer of neutral liquid petrolatum placed on top of the liquid, by blowing into a hollow glass tube in the other hole of the rubber stopper the syphon was started.

Making up the solution by using distilled water from which the air and $CO_2$ are expelled, allowing to stand until decomposition and precipitation have taken place, covering with a layer of liquid petrolatum and syphoning off the quantities of solution required, make an ideal method of handling not only this volumetric solution but very many others, it being our practice to follow this method whenever possible.

Research and Analytical Department,
Riker Laboratories.

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## ON THE BLUE HYDROCARBON OCCURRING IN SOME ESSENTIAL OILS.[1]

[Preliminary Note.]

By Alfred E. Sherndal.

Scattered through the literature of the essential oils are frequent descriptions of blue fractions obtained in the distillation of various oils, the most intensely colored sections distilling between the temperatures, 275° and 300°, or higher. A few oils, such as those of chamomile, worm-wood, and cubebs, are notable for their blue or green color before fractionation.

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[1] Reprinted from *Jour. Amer. Chem. Soc.*, 1915, p. 167.

In a few instances where intensely colored fractions have been obtained, the investigators have thought themselves in the possession of a pure substance.[2] In most cases, however, they have recognized that the color is due to the presence of some colored substance other than the bodies making up the bulk of the oil, and the usually accepted view has been, that this is an oxygenated substance related to the sesquiterpene alcohols.[3]

Semmler [4] has summarized the literature covering these oils, and remarks that there are two views possible in regard to the blue fractions: either the greater part is colorless, and appears colored owing to the presence of a small amount of an intensely blue substance, or the sections boiling between 275° and 300° are actually composed principally of a blue compound. That the latter is not the case, however, is evident from a survey of the literature, since the only purification method resorted to is a fractionation out of oils which contain large amounts of sesquiterpenes and sesquiterpene alcohols, with boiling-points also ranging from 250° to 300°. For the same reason no importance can be assigned to the various analyses of the blue fractions.

Blue products have also been obtained in the laboratory by various reactions, usually from oils composed principally of sesquiterpenes and sesquiterpene alcohols. In such cases, there seems always to have taken place a dehydration and subsequent oxidation of a sesquiterpene alcohol, or a direct oxidation of a sesquiterpene. For example, Wallach and Tuttle,[5] by the action of phosphoric anhydride, or zinc chloride on guaiol, the alcohol of guaiac-wood oil, obtained a blue sesquiterpene. They considered the color to be due to the presence of a small amount of an oxidation product. On the other hand, Gadamer and Amenomija [6] obtained a guaiene without blue color, by dehydrating guaiol with potassium acid sulfate.

An interesting observation was made by Hentschel and Wislicenus,[7] who found, on rectifying the products of the dry distillation of calcium adipate, that the fraction boiling between 135° and 145° at 30 mm. had a blue color resembling that of Roman chamomile.

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[2] Piesse, "Art of Perfumery," **1879**, p. 57.
[3] Bartelt, "Die Terpene und Campherarten," **1908**, p. 4.
[4] *Die Aetherischen Ole*, **3**, p. 260.
[5] *Ann.*, **279**, 379 (1894).
[6] *Archiv. der pharm.*, **241**, 33 (1903).
[7] *Ann.*, **275**, 312 (1893).

Semmler and Jakubowicz [8] obtained blue oils by heating the gurjunene sesquiterpenes in autoclaves filled with air or oxygen.

So far as the writer knows, no connection has as yet been assumed between the blue oils, and the striking color reactions which have frequently been observed when oils consisting largely of sesquiterpenes or sesquiterpene alcohols are treated in dilute solutions with mineral acids. An experiment seems, however, to indicate that such connection may exist. If oil of gurjun balsam be dissolved in acetic anhydride, and a small amount of sulfuric acid added, the mixture becomes intensely blue, and on diluting with water and distilling the oil in a current of steam, a deep blue distillate is obtained.

Very many oils containing sesquiterpenes and related compounds give strong color reactions when dissolved in acetic anhydride containing a trace of sulfuric acid. Of the oils examined in this laboratory, those of gurjun, amyris, and guaiac-wood give strong blue or violet colors under these conditions; santal and cedar-wood, none. This test may be used to advantage to detect adulterants in some oils, such as santal.

As to the nature of this blue constituent, nothing whatever has so far been definitely ascertained, for the reason that, as already indicated, it has not been isolated in a state of even approximate purity. A remarkable fact is that a substance with such intense color should possess a comparatively low boiling-point, indicating a simple molecule. Semmler [9] suggests the possibility of a bimolecular structure, closely related to the sesquiterpenes, which on distillation dissociates, and on condensing, again forms a bimolecular compound, with a group similar to that in indigo: $>C : C<$. As a rule, however, the assumption has been made that the blue substance is an oxygenated compound of alcoholic nature.

The following work describes the isolation of this body in a state of purity, as shown by the analysis and reactions. As a pure substance, its remarkable properties become even more striking than before. The analysis shows it to be a highly unsaturated hydrocarbon, but the peculiar grouping of atoms to which it owes its unique properties is more difficult to speculate upon than ever.

The property which was utilized to isolate the substance, and which has heretofore not been noted, is its solubility in mineral acids of certain strengths. The method of preparation was as follows:

[8] *Ber.* **47**, 2252–9 (1914).
[9] *Aetherischen Ole*, **3**, p. 266.

Fifty grams of a very blue fraction, freshly steam distilled, were shaken with 10 g. of 63 per cent. sulfuric acid, and the mixture allowed to settle over night. The acid layer was then drawn off, diluted with water, and extracted with petroleum benzine until no more blue color was taken up. The benzine solution, dark blue in color, was then shaken out with 85 per cent. phosphoric acid until no longer blue, the dark red acid solution drawn off, diluted with water, and extracted with ether. The residue from the evaporation of the ether amounted to 0.141 g., or 0.28 per cent. This, redissolved in 50 g. of a pale yellow oil, gave a mixture with about the same tint as the original, showing that there was no appreciable loss in the preparation.

Larger quantities, isolated in this way, were further purified by distillation with steam, and finally *in vacuo*. The substance thus obtained was a slightly viscid liquid, intensely blue in thin layers, black in quantity, with a weak phenolic odor, suggesting thymol, especially when warm.

Subst., 0.2118 and 0.2294 g. gave $CO_2$ 0.7054 and 0.7587 g.; $H_2O$, 0.1478 and 0.1903 g.; calc. for $C_{15}H_{18}$: C = 90.84; H = 9.15; found: C = 90.83 and 90.20; H = 9.23 and 9.28.

The molecular weight determination was made by Dr. Earl F. Farnau of New University, by the cryoscopic method, using benzene as solvent. Found: 187.2 and 193.4 (av., 190.3); calc. for $C_{15}H_{12}$: 1.98.

The compound is, then, a hydrocarbon, having most probably the formula $C_{15}H_{18}$, and for it the writer would preserve the name "azulene," proposed in 1863 by Piesse,[10] one of the earliest investigators, for the blue fraction which he obtained from oil of wormwood.

The specific gravity at 25° is 0.9738, when freshly steam-distilled. Exposed to light and air, it is gradually converted into a brown resin. Distilled at atmospheric pressure, the boiling-point rises from 295° to 300°, leaving a tarry residue, soluble in ether with a brown color. At about 25 mm. azulene distils from 185° to 195°, leaving a brown residue of about 5 per cent. Since the product had been previously distilled with steam, this shows that it cannot be distilled without change under these conditions. When evaporated on the water-bath in an open dish, a brown resin, amounting to 10 per cent. or more, remains.

[10] *Compt. rend.* **57**, 1016 (1864).

Azulene is readily soluble in most organic solvents. In 95 per cent. alcohol it is miscible in all proportions; in more dilute alcohol the solubility is much less, but even 50 per cent. alcohol takes up enough to be tinted, a decided blue.

Its solubility in strong inorganic acids, which makes its isolation possible, is especially remarkable. In 60 to 65 per cent. sulfuric acid, azulene dissolves to a clear yellow, strongly fluorescent solution; on dilution with water, it is thrown out again as a blue oil, apparently unchanged. It also dissolves in 50 per cent. sulfuric acid, but less readily. The solution in phosphoric acid is remarkable for its fluorescence: reddish yellow by transmitted light, intense apple green by reflected light. These acid solutions can be extracted with benzine without removing any azulene, and by repeating several times, a product can be obtained, free from sesquiterpenes or alcohols.

Azulene is strongly resistant to the action of even strong sulfuric acid. When heated with two parts of 94 per cent. acid for fifteen hours on the water-bath, a dark brown solution results, which, on diluting with water, again yields the blue oil. Strong formic acid dissolves it with a green color, but in acetic acid the color remains unchanged, as in the neutral solvents. On mixing dry ether solutions of azulene and hydrochloric acid, no change in color was observed.

Nitric acid in acetic acid solution produces yellow amorphous substances, not further examined.

The oxidation of azulene with permanganate has so far yielded only lower fatty acids.

It is not attacked by sodium in hot alcohol, nor does heating with strong alkali affect the color.

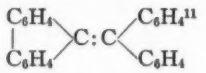
By the action of acetic anhydride and sulfuric acid, a substance was obtained, evidently a sulfonic derivative, which was soluble in water. On adding sodium carbonate in excess a sodium salt separated out, which was recrystallized from hot water. The water solution of the salt is colored violet, and changes to a light green on acidifying. If then shaken with ether, the latter becomes violet, and this color is again taken out by shaking with alkali.

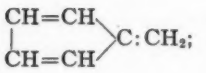
The sodium salt, on heating, gives off blue fumes which condense to a blue oil; at the same time sulfur dioxide is liberated.

On standing three months in a corked bottle, a preparation of the sodium salt had decomposed into a mixture of oil and resin.

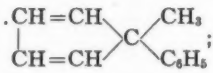
The water solution gives blue precipitates with barium and calcium solutions, and is decolorized by bromine water.

It appears established that azulene is closely related to the sesquiterpenes. From no other class of compounds have hydrocarbons been obtained which show such intense color. Colored hydrocarbons which have so far been prepared are characterized by complex structure or a dense arrangement of the atoms, the intensity of the color increasing with the size of the molecule; for example:

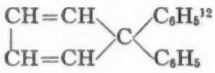




1. Yellow.



2. Red liquid.



3. Deep red solid.

Rubicen, a red hydrocarbon, $C_{26}H_{14}$, m. p. 306°.[13]

It is obvious that in azulene we have an entirely different and unique chemical compound. We hope, in a subsequent communication, to collect further data on this interesting substance.

The writer wishes here to acknowledge his indebtedness to Dr. Francis D. Dodge for helpful suggestions as well as for aid in obtaining material used in connection with the above work.

Laboratory of the Dodge and Olcott Company, Bayonne, N. J.

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## DEXTRINIZED MALT IN INFANT-FEEDING.[1]

By Theodore Le Boutillier, M.D.

During the last two years a study has been made in the service of Dr. Howard Childs Carpenter in the Children's Department of the Philadelphia General Hospital of the result of adding dextrinized malt to milk-mixtures in infant-feeding, replacing the lactose formerly used. While the cases studied have been too few in number and cover too short a period of time to justify any absolute statements, the general conclusions reached may be found helpful.

In the cases of malnutrition in which a rational milk-mixture has been employed, but the weight has remained practically stationary, we have found in most instances that the substitution of dextri-

[11] Graebe, *Ber.*, **26**, 2334 (1892); **25**, 3146 (1891).

[12] Thiele, *Ber.*, **33**, 668, 851, 3395 (1900); *Ibid.*, **36**, 842 (1903); *Ann.*, **319**, 226 (1901).

[13] Plummerer, *Ber.*, **45**, 294 (1912).

[1] Reprinted from Philadelphia General Hospital Reports, vol. ix, p. 157.

maltose for lactose has been of much benefit in assisting assimilation of the carbohydrate, and in increasing the weight of the baby, the carbohydrate percentage varying between five and seven in these cases.

In another series in which a normal carbohydrate percentage (6) has resulted in sugar-indigestion, with fermentation and diarrhœa, we have found that with the same percentage of dextri-maltose, the majority of the cases clear up rapidly, even those in which the lactose had been first reduced to three or four per cent. and gradually increased, but with the symptoms of indigestion persisting. In cases of simple diarrhœa in infancy the malt-sugar has a much more beneficial effect than milk-sugar, and it can certainly be borne in higher percentages. In the majority of cases malt-sugar appears to be slightly constipating; but it is of interest to note that in a few cases of malnutrition, in which the bowels have been constipated and movements have been secured only by the employment of enemata or by mechanical means, after a few days of the use of dextri-maltose in the feeding, the proportion of fat and proteid remaining the same, but the sugar being increased to six or seven per cent., the stools become less hard and of a better consistency. This is true, however, only of certain cases, for in that of other infants with constipation the stools have become slightly more constipated.

It would seem, therefore, that malt-sugar has marked advantage over either milk-sugar or cane-sugar in the feeding of infants unable to assimilate or thoroughly digest the milk-sugar or cane-sugar, and in the feeding of infants suffering from diarrhœa.

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## AN EXPERIMENTAL STUDY OF A NEW REMEDIAL AGENT AND OF ITS EFFECTS IN PULMONARY TUBERCULOSIS.[1]

By Bertram H. Waters, M.A., M.D., New York.

The employment of inhalations, in the treatment of pathological conditions of the respiratory tract, has appealed to many as a rational therapeutic procedure, and medical literature is replete with descriptions of generators, vaporizers, and pneumatic cabinets, together with the various substances thought to possess remedial properties, which have been employed. A review of this literature

[1] Reprinted from *Medical Record*, February 13, 1915.

is interesting, showing that from the earliest times the subject of inhalation has held an important place. As early as 1664 this method was applied by Bennett in the treatment of pulmonary tuberculosis. Laennec in 1810 employed it with considerable success; Schneider and Valz constructed the first nebulizer in 1829, and Auphan applied pulverization and nebulization in the treatment of chronic diseases of the respiratory tract in 1847. About the same year Salles-Girons established an inhalatorium at Pierrefonds, and for the first time the question was raised of the possibility of reaching the lungs by these methods. A lively discussion followed, and repeated experiments by such investigators as Dumarquay, Fournie, Bourouilloux, Gratiolet and Travenier, Poggiale, Gerhardt, Waldenburg, and Solis-Cohen have finally demonstrated that by pulverization and nebulization remedies may be efficiently administered, the latter observer even going so far as to state that a physician had not done his full duty, in some cases, unless he resorted to such methods. Many other studies of this subject have been made, among the more recent being those of Heryng (1902), Freund (1907), Foxwell (1907), Cointet (1909), and Bulling (1909), the general result of which has been one of approval. Though the therapeutic and even the germicidal action of inhaled sprays, especially, has been confirmed, such action seems to be limited to the surface of the respiratory mucous membrane, and the influence upon pathogenic conditions, such as tubercle, in the lung tissue, is very problematic.

The ethereal oils and the balsams have been found to be the most useful substances for inhalation, oil of turpentine, oil of eucalyptus, oil of cade, the balsams of Peru and Tolu, and creosote having been employed with more or less success, either in vapor form or nebulized by means of atomizers and nebulizers.

Oil of turpentine and some of the other volatile oils owe their therapeutic value to terpenes. The terpenes are hydrocarbons having the composition represented by $C_{10}H_{16}$, or some multiple of that formula. The principle common to all terpenes is *pinene*. It is a constituent of the volatile oils of the pine family and of several other families of plants. This study deals not with turpentine, the complex oleoresin of the pine tree, but with its chief constituent, pinene. To it are attributed the physiologic and therapeutic actions of oil of turpentine.

Locally, pinene is a powerful stimulant to the skin and mucous membranes. It is also antiseptic and bactericidal, and appears to be

especially antagonistic to the typhoid bacillus. When taken by a healthy person, in moderate doses, it produces a sense of warmth in the stomach, soon followed by exhilaration, and, if the amount be sufficient, giddiness and even a species of intoxication. The pulse is increased in force and frequency. Pinene is excreted through the lungs and kidneys, and its irritant action upon the latter and upon the genito-urinary tract is very decided.

Oil of turpentine, on account of the pinene it contains, has acquired a reputation as a hæmostatic in passive hemorrhage from the stomach, intestine, lung, and uterus. It is often very efficient in ulceration of the bowels when taken by the stomach, probably acting locally in the intestine, and in old gastric ulcers good results are sometimes derived from its use. It is given internally as a diffusible stimulant of especial value in exhausting fevers. It has long enjoyed high repute as a remedy for the treatment of typhoid fever, especially if diarrhœa persists and relapses occur, indicating unhealed ulceration of Peyer's patches. Locally it is very useful as a counterirritant in pleurisy and bronchitis, applied in the form of turpentine stupes. Probably some of the benefits derived from turpentine stupes in pneumonia are due to inhalation of its vapor.

Standing in the way of a more general use of oil of turpentine as a remedial agent is its irritant action upon the kidneys and urinary tract. When its vapor is inhaled it is readily absorbed, and instances are recorded in which persons engaged in the turpentine industries have experienced renal inflammation.

When the vapor of pinene is exposed to a current of ozonized air, prepared by the action upon dry air of a high-tension electrical discharge, an addition occurs between the pinene and oxygen, resulting in the production of a dense white vapor. To this substance I have given the name oxypinene, a convenient general term, descriptive of all combinations of pinene with oxygen, either as $O_2$ or $O_3$. It is, however, chemically a pinene monozonide, occurs also as a diozonide and other multiples of the oxygen atom, and readily dissociates into its active principles, peroxide of hydrogen, pinene aldehyde and ketone and pinonic acid.

It possesses the valuable therapeutic properties of pinene without its irritating effects upon the kidneys and urinary tract. Applied to the skin and mucous membranes it acts as a mild stimulant, markedly differing in this respect from the powerfully irritating oil of turpentine. The vapor is respirable for hours at a time, and its use

may be continued indefinitely day after day without producing symptoms of renal irritation. It is antiseptic and bactericidal when applied to cutaneous and mucous surfaces.

*Antiseptic and Germicidal Properties of Oxypinene.*—From pure broth cultures of typhoid, diphtheria, and colon bacilli, and staphylococcus, smears were made on cover-slips. These were thoroughly dried in the incubator, and placed under a bell-jar, into which oxypinene was allowed to enter through an opening near its base, and escape through an opening at the top which was lightly plugged with cotton. At intervals of forty minutes, one hour, one and a half hours, and two hours, a smear of each culture was removed and dropped into broth tubes. After incubation all the controls except that of diphtheria showed growth. All exposed smears produced growth except those of diphtheria.

The same organisms were used, but instead of incubator-dried smears, large drops of broth cultures of each on cover-slips were exposed, in the same manner as previously, for fifty minutes, seventy minutes, and one hour and fifty minutes. After incubation, all controls showed marked growth. All exposed drops failed to produce growth, except that of staphylococcus, growth of which was markedly retarded and very slight. As all the exposed drops became dry before the expiration of forty minutes, and as in the previous experiment none of the incubator-dried smears were killed, it was concluded either that the organisms in all exposed drops were killed under forty minutes, or that at least some moisture is necessary to obtain a germicidal effect. As on theoretical grounds the latter supposition seemed probable, the use of incubator-dried preparations was abandoned.

Agar-agar, in Petri plates, was substituted for cover-slips, and upon the surfaces of these, broth cultures of the organisms already used were planted in streaks. These plates were then exposed in the manner already described for one and one-half hours. All controls showed marked growth after twenty-four hours' incubation. All exposed plates produced no growth after five days' incubation.

Large drops of broth culture of the typhoid bacillus, after exposure on cover-slips in the manner described, for twenty-five and forty minutes, were smeared upon agar-agar slant tubes. The controls showed marked growth after eighteen hours' incubation. The tubes inoculated with culture which had been exposed for twenty-five minutes showed marked growth after twenty-four hours' incuba-

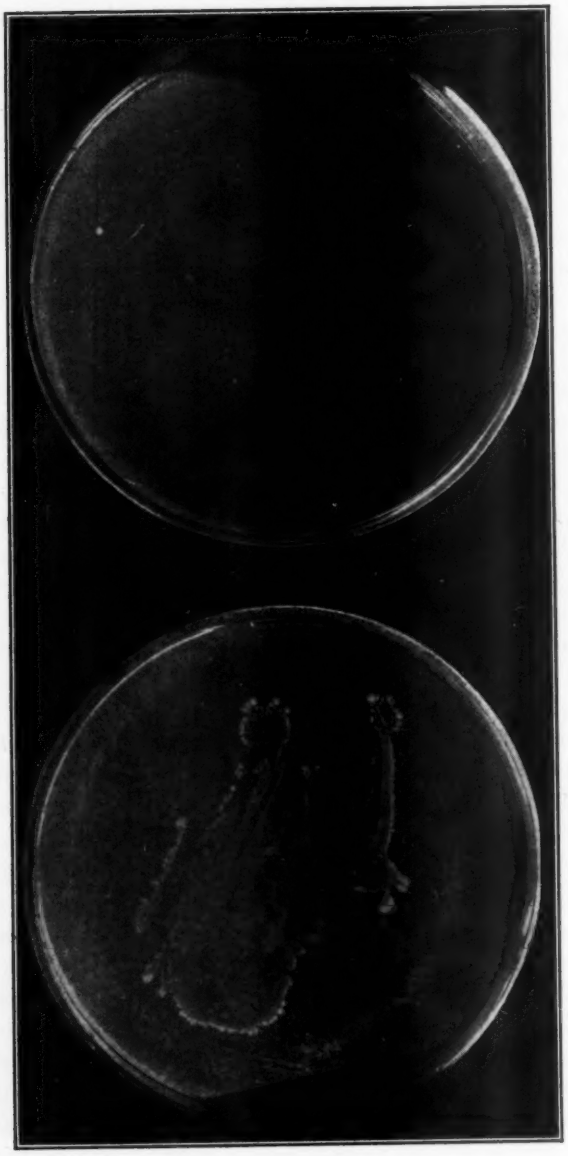
tion. The tubes inoculated with culture which had been exposed for forty minutes showed no growth after ninety-six hours' incubation.

Large drops of broth culture of each of the organisms previously used were exposed in the same manner and for the same periods as in the preceding experiment, and planted on agar-agar slant tubes. The controls showed marked growth after eighteen hours' incubation. The tubes inoculated with culture which had been exposed for twenty-five minutes showed growth after twenty-four hours' incubation. The tubes inoculated with culture which had been exposed for forty minutes showed no growth after ninety-six hours' incubation.

The conclusion seemed to be justified that for typhoid, diphtheria, and colon bacilli, and the staphylococcus, in pure broth culture, when even the slightest moisture is present, oxypinene is germicidal in from twenty-five to forty minutes.

Upon the surface of agar-agar, in Petri plates, broth cultures of subtilis, anthrax, and pneumococcus were planted in streaks. These plates were exposed in the manner already described for one and one-half hours. The controls showed marked growth after eighteen hours' incubation. The exposed plates showed no growth after forty-eight hours' incubation. At the end of five days no growth had appeared.

Upon the surface of agar-agar, in Petri plates, broth cultures of typhoid, diphtheria, and anthrax bacilli, and staphylococcus were planted in streaks. These plates were exposed for two and one-half hours, not under the bell-jar, *but in a room* having a cubic capacity of about 2500 feet. The room was fairly well filled with oxypinene. The controls showed marked growth after eighteen hours' incubation. The exposed plates, after twenty-four hours' incubation, showed no growth, except that of staphylococcus, on which a very slight growth appeared. After forty-eight hours' incubation, anthrax seemed to show slight growth, but at the end of seventy-two hours it had not spread, and a smear of it planted on an agar slant tube failed to produce growth. A single agar Petri plate, on the surface of which the same organisms, in broth culture, had been streaked, was exposed under the bell-jar for two hours, and failed to show growth of any organism, after seventy-two hours' incubation, while anthrax overgrew all other growths, on the control plate, after twenty-eight hours' incubation.



B

A

FIG. 1.—*Micrococcus pyogenes aureus*: A, control plate; B, exposed plate.

These experiments have been repeated many times, in the same manner, with uniform results, and from them it seems conclusive that oxypinene is a germicidal gas, of high efficiency, which is at once respirable and easily produced, continuously, in large quantities.

Figs. 1 and 2 are photographs from agar-agar Petri plates upon which were planted pure cultures of *M. pyogenes aureus* and *B. anthracis.* Similar experiments with similar results were made with cultures of *B. typhosus, B. coli communis,* and *B. subtilis,* but lack of space has necessitated our omission of illustrations of the same. These plates were exposed to the action of oxypinene for two and one-half hours, in a room of about 2500 cubic feet capacity, in which the generator was constantly operating and keeping it fairly well filled. Control plates were made of each organism, and both exposed and control plates were incubated for seventy-two hours.

*Clinical.*—Observations were made of twenty-one patients. As with two exceptions they were of the dispensary class, they were difficult to control for so long a period as could be desired, some insisting upon their discharge with the alleviation or disappearance of their active symptoms. With the exception of Case V, a very early tuberculous infection, and Case XXI, a child ill with pertussis, following an unresolved bronchopneumonia, all were in the second or third stage of pulmonary tuberculosis (Classification of the National Association for the Study and Prevention of Tuberculosis), and tubercle bacilli were demonstrated in the sputum. It seemed desirable to select lesions of such severity, but equally so that they should offer some hope of improvement, in order that, so far as possible, the amelioration of symptoms which so often follow any change in environment and dietetic régime might be discounted. However, to study fully the effects of oxypinene upon special symptomatic features or types of disease, such as active hemorrhage, marked pyrexia, constant dyspnœa, tuberculous laryngitis, acute phthisis, chronic pulmonary tuberculosis, and the toxæmia of extensive cavitation with secondary infection, certain patients were admitted to treatment whose prognosis seemed hopeless, and who, though showing for a time the beneficial effects so generally observed in the others, finally died. With the exception of Cases XX and XXI, who were treated in their own homes, the entire group was observed in a private hospital in the city for three months, and thereafter for five and one-half months in a private sanatorium in the country. The periods of observation varied from nine days to nine months. With

a few exceptions all were studied according to the following routine: Each was observed in bed, for forty-eight hours before beginning treatment, during which time two hourly records of temperature (rectal), pulse, and respiration were made, twenty-four total amounts of urine and sputum examined, and a hæmoglobin estimation and differential blood count made, in addition to a complete physical examination. Thereafter temperature (rectal), pulse, and respiration were recorded every twenty-four hours or twice daily, weights were taken, twenty-four-hour total amounts of urine and sputum examined, and a hæmoglobin estimation and differential blood count made weekly. Twenty-four-hour total records were also kept of urine and sputum daily. Physical examinations were made at frequent intervals, and at least once a month. The patients were in bed or up and about, as their temperatures or general condition required, and no other treatment was given, except cathartics, and heroin or codeine occasionally. In some instances an iron preparation was used to study the behavior of the hæmoglobin. The diet consisted of three wholesome meals daily, and one raw egg in one glass of milk twice daily. Partly through circumstance, partly with the design of checking up and controlling results, the period of observation was divided into three epochs: the first, for three months, in the city; the second, for two and one-half months, in a sanatorium in New York, at an elevation of 1500 feet; and the third, for three months, in a sanatorium in New Jersey, at slight (500 feet) elevation. During these epochs an opportunity was afforded of observing and contrasting the effects of ideal sanatorium régime without, and also with, oxypinene treatment. In no other respects were the routine and conditions of observation varied. During the first epoch treatment was given continuously, with only sufficient open air for proper ventilation, and several of the patients had no direct sunlight, their windows opening on a court. During the second and third epochs treatment, when given at all, was continuous during the night, and for periods of from one to two hours twice during the day, the remainder of the time being spent in the open air. The blood, sputum, and urine examinations were made by the Lederle Laboratories, the Higgins Laboratories, and by my assistant and resident, Dr. W. A. Glanville. While there is probably some variation of results because of differing personal equation, they have been so checked up as to make this negligible, and in Cases XX and XXI all these examinations have been made by the same examiner.

The following indicates the types of cases studied:

| | Stage I. | Stage II. | Stage III. |
|---|---|---|---|
| Number of cases. . . | 1 (Case V) | 4 (Cases XIII, XIV, XVI, XVII) | 15 (all other cases) |

The other case, XXI, was the child referred to with pertussis, following an unresolved, possibly tuberculous, bronchopneumonia.

As space is lacking for a detailed description of each of these, a brief synopsis of several, together with the blood findings, and the temperature curves of two, are given. These are average cases, and illustrate the points noted.

CASE I.—Woman, 34 years, Stage III, improved. General condition poor. Extensive infiltration, both upper lobes with softening, especially on left side, where there is well marked cavitation. Complicating nephritis. Moderately toxic. Sputum positive.

| Red cells. | Hb. | White cells. | Weight. | |
|---|---|---|---|---|
| 3,750,000 | 75 | 8,200 | 96 | Before treatment. |
| 4,960.000 | 81 | 13,600 | 101¼ | After one month's treatment. |

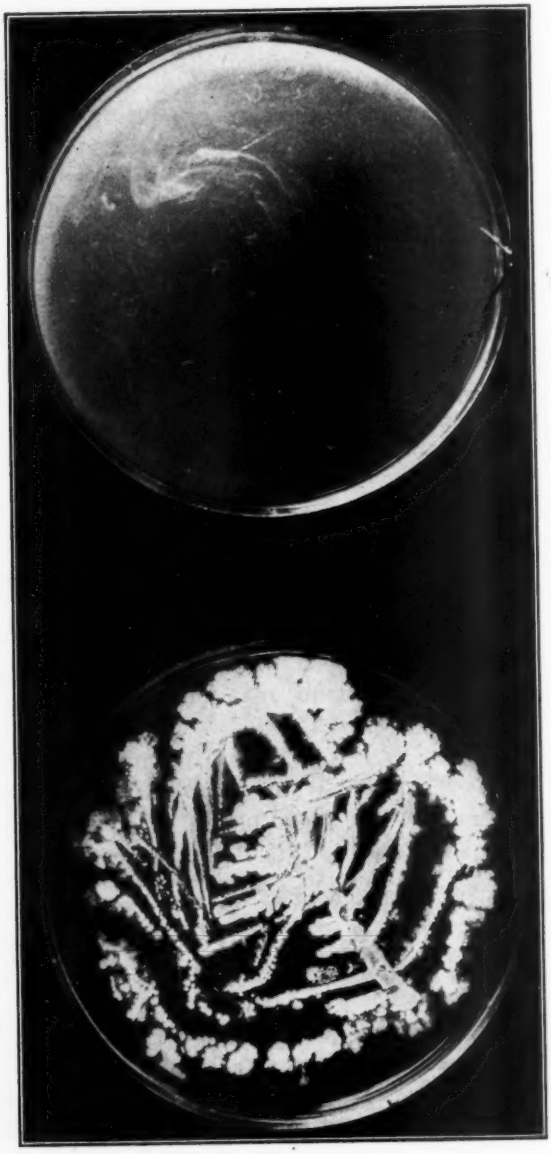
Constant racking cough, with thick, tenacious sputum. Sputum increased from 15 Cc. to about 150 Cc. daily with relief of cough. Discontinued treatment against advice, because of being needed at home, and, her condition becoming again progressive, she died eight months later.

CASE VI.—Woman, 24 years, Stage III, arrested. General condition poor. Fairly diffuse infiltration, right lung with softening in upper lobe anteriorly. Thickened pleura with adhesions, lower portion. Infiltration left apex. Little toxæmia. Sputum positive.

| Red cells. | Hb. | White cells. | Weight. | |
|---|---|---|---|---|
| 4,100,000 | 75 | 10,000 | 84 | Before treatment. |
| 5,100,000 | 92 | 13,300 | 99 | After six weeks' treatment. |
| 5,552,000 | 78 | 15,060 | 103½ | After 7½ months' treatment. |

These cases illustrate the effect upon the sputum with relief of cough, the changes in the blood picture, and, what is usually observed and is an indication of such result, a white cell count, which remains high in favorable and arrested cases. In several instances, though not uniformly, the hæmoglobin percentage has fallen after ceasing treatment.

CASE VII.—Woman, 24 years, Stage III, improved. General condition fair. Infiltration right upper lobe without softening. Diffuse



B

A

FIG. 2.—*Bacillus anthracis:* A, control plate; B, exposed plate.

infiltration left upper lobe with cavitation. Complicating emphysema and general bronchitis. Little toxæmia. Sputum positive.

| Red cells. | Hb. | White cells. | Weight. | |
|---|---|---|---|---|
| 4,400,000 | 86 | 7,200 | 137½ | Before treatment. |
| 5,170,000 | 92 | 12,100 | 153½ | After 2½ months' treatment. |
| 4,860,000 | 82 | 12,800 | 149¼ | After 5½ months' treatment. |

During the last three months treatment, which had been continuous, was interrupted, but patient was under sanatorium régime in the country. She was then admitted to a sanatorium where previously she had been refused admission on account of the extent of her lesion.

CASE XII.—Man, 41 years, Stage III, improved, approaching arrest. General condition fair. Infiltration both upper lobes, with areas of softening and fibrosis; small cavity in right upper; left lung adherent at base; left chest much contracted. Complicating chronic bronchitis of years' duration. Little toxæmia. Sputum positive.

| Red cells. | Hb. | White cells. | Weight. | |
|---|---|---|---|---|
| 4,790,000 | 81 | 11,600 | 115¼ | Before treatment. |
| 5,942,000 | 91 | 10,420 | 116½ | After 5 months' treatment. |

Tubercle bacilli disappeared from the slight morning sputum, and he returned to employment.

CASE XIII.—Man, 28 years, Stage II, arrested. General condition fair. Extensive infiltration right upper and middle lobes, with softening in the upper. Infiltration left apex. Moderate toxæmia. Sputum positive.

| Red cells. | Hb. | White cells. | Weight. | |
|---|---|---|---|---|
| 4,780,000 | 81 | 9,200 | 119¾ | Before treatment. |
| 6,588,000 | 85 | 13,200 | 122 | After 6 months' treatment. |

Returned to employment.

CASE XV.—Man, 21 years, Stage III, improved, approaching arrest. General condition poor. Infiltration right upper lobe, and scattered areas throughout left lung, with softening in upper lobe. Considerable toxæmia. Sputum positive.

| Red cells. | Hb. | White cells. | Weight. | |
|---|---|---|---|---|
| 3,480,000 | 66 | 22,400 | 116 | Before treatment. |
| 5,736,000 | 73 | 12,400 | 118½ | After 3¼ months' treatment. |

As he felt well he refused longer to continue treatment and returned home. Lesion still active. Tubercle bacilli were reduced in number and all secondary organisms had disappeared.

CASE XVI.—Man, 28 years, Stage II, arrested. General condition poor. Diffuse infiltration right upper lobe, with softening. Scattered infiltration throughout rest of lung. Infiltration left apex. Considerable toxæmia. Sputum positive.

| Red cells. | Hb. | White cells. | Weight. | |
|---|---|---|---|---|
| 3,410,000 | 66 | 7,600 | 109 | Before treatment. |
| 5,530,000 | 96 | 12,220 | 110 | After 2½ months' treatment. |
| 6,422,600 | 104 | 14,210 | 115¾ | After 3¾ months' treatment. |

Interesting in that for two and one-half months he received no inhalations, but was under sanatorium régime in the country. Inhalations were begun there, and after two months he returned to employment. Slight morning cough persisted with about 5 Cc. of sputum daily, from which tubercle bacilli and all secondary organisms had disappeared.

CASE XXI.—Child, 2½ years. Pneumonia two months previously, coughing continuing with failing health. Apparently had pertussis. General condition extremely poor; pale, languid, and apathetic. Respiration 60, pulse uncountable, a feeble cough with each expiration. Both lungs full of moist râles. Over right lower lobe voice intensified and respiration bronchovesicular.

| Red cells. | Hb. | White cells. | Polys. | Lymphs. | |
|---|---|---|---|---|---|
| 5,536,000 | 62 | 84,000 | 62.8 | 34.6 | Before treatment. |
| 5,460,000 | 70 | 27,000 | 34.0 | 53.6 | After 9 days' treatment. |
| 5,480,000 | 79 | 39,000 | 41.0 | 54.4 | After 16 days' treatment. |

Apparently made perfect recovery. Reported well since.

CASE XX.—Man, 41 years, Stage III, improved. General condition fair for duration of disease (eight years). Nutrition had been well maintained. Infiltration right upper lobe. Extensive diffuse infiltration entire left lung, with large cavities in both lobes.

| Red cells | Hb. | White cells | Average daily urine, Cc. | Per cent. urea, gm. | Weekly sputum, oz. | Hours' treatment monthly |
|---|---|---|---|---|---|---|
| 4,368,000 | 74 | 24,100 | 350 | 10.5 | 90 | Before |
| 4,480,000 | 80 | 30,500 | 425 | 32.4 | 142 | 174 |
| 4,960,000 | 86 | 14,400 | 980 | 19.4 | 92½ | 152¼ |
| 5,984,000 | 84 | 19,200 | 1,023 | 14.2 | 85 | 144¼ |
| 4,860,000 | 78 | 22,000 | 773 | 17.6 | 87 | 121 |
| 5,920,000 | 76 | 16,400 | 807 | 29.2 | 90 | 88½ |
| 5,620,000 | 73 | 17,400 | 883 | 25.4 | 87 | 67½ |
| 6,208,000 | 72 | 23,200 | .... | 18.2 | 87 | ..... |
| 5,800,000 | 75 | 20,000 | .... | 17.4 | .... | ..... |

After completing a second sanatorium course returned home and for fourteen months previous to treatment had been confined to bed. During treatment toxæmia was reduced, there were no hyperidroses, and, after the fourth month, no rigors. He was able to be dressed and about his rooms, and to do something for himself. The enormous cavities continued large daily secretions and were a constant source of exhaustion. A permanently favorable result could scarcely be expected. Tubercle bacilli greatly diminished in number, and all secondary forms disappeared. Improvement continued and he was able to return to business for part of the day.

The results of treatment may be indicated as follows:

| | Stage I. | Stage II. | Stage III. |
|---|---|---|---|
| Unimproved | | | 1 (Case III) |
| Improved | 1 (Case V) | 2 (Cases XVI, XVII) | 9 (Cases I, VII, VIII, IX, XII, XV, XVIII, XIX, XX) |
| Arrested | | 2 (Cases XIII, XVI) | 1 (Case VI) |
| Died | | | 4 (Cases II, IV, X, XI) |

Case XXI was markedly improved.

This classification is conservative, as, of the Stage II cases, one (Case XVII) reported as improved was in a condition approaching arrest, but would not remain longer under observation, and of the Stage III cases, three (Cases XII, XV, and XIX) reported as improved were also in a condition approaching arrest, and two of them have returned to employment.

Accurate studies of the blood of tuberculous patients are of comparatively recent date. While many observations are recorded in the literature, they are confused by a lack of agreement among the reporters, either in their technic or in their identification and classification of the several cellular constituents of the blood, or in their interpretation of the frequent and often rapid variations noted in their numbers and forms. Even to-day, with our fuller knowledge of hæmatology, the personal equation of the examiner influences considerably a differential count, and there is more or less difference of opinion among hæmatologists as to the meaning of certain findings. What are probably the first entirely reliable studies were made by Ullom and Craig. From observation of thirty-nine patients reported in 1906, they conclude:

1. In pulmonary tuberculosis, without cavity formation, a mild anæmia, with a decrease in erythrocytes and a relatively greater decrease in hæmoglobin, is constant.

2. From the standpoint of prognosis, an increase of the erythrocytes, in cases without cavity formation, is of favorable significance.

3. In advanced cases a decrease of the leucocytes is of unfavorable import.

4. In our investigations we have received the impression that the actual increase of lymphocytes seems to correspond to the increase of resistance on the part of the organism to the tuberculous infection, but further study is required to confirm this deduction.

5. The transitionals seem to follow the same rule as the lymphocytes in this regard.

6. At the beginning of the investigation the eosinophiles seemed to increase with the patient's improvement, but further study did not support this view.

Curry, in studying the effect of altitude upon the blood, found in normal and tuberculous individuals an increase in red and white corpuscles, but notes little variation in the different kinds of leucocytes, while Webb and Williams have shown an increase in the proportion of the mononuclear cells in normal persons, and in cured, stationary, and improving tuberculosis. That under various forms of treatment the blood findings correspond closely with those of Ullom and Craig has been shown by Solis-Cohen and Strickler, who from 182 blood counts of fifty tuberculous patients treated with Bier's hyperæmia, blisters, iodoform, creosote carbonate, and nuclein observe that there is an increase in the proportion of lymphocytes and of polynuclear cells with one or two nuclei. These investigators have previously reported that the percentage of lymphocytes was increased in incipient, moderately advanced, and improving cases, and that the percentage of large mononuclears and transitional cells, while within normal limits, was greatest in incipient and improving cases.

The findings of my own series of cases of twenty-one patients are largely in accord with these observations and seem to indicate that:

1. The percentage of hæmoglobin (Tallquist scale, controlled by von Fleishl or Dare hæmoglobinometer) was reduced. It was increased under treatment. This increase did not seem to depend upon the administration of iron.

2. The erythrocytes were reduced in number. They increased under treatment, at least temporarily, irrespective of the lesion.

3. When marked leucocytosis existed, due to toxæmia, it was reduced. When the number of leucocytes was below normal, it was increased by treatment.

4. The lymphocytes were usually reduced, and were increased and remained so in those patients who improved. It seems probable that this increase may be considered as a reliable indication from a prognostic standpoint.

5. The large mononuclears seem to follow the curve of the lymphocytes. It seems probable that they may be included with them, and that their increase or decrease may have a like significance.

6. No conclusion could be drawn from the behavior of the transitionals, eosinophiles, or basophiles.

7. The classification and grouping of the polynuclear neutrophiles according to von Arneth's method seems to have some prognostic value.

To summarize, there seems to be, under this method of treatment of pulmonary tuberculosis, and temporarily at least, even in the progressive and fatal types of the disease, a distinct and constant tendency of the cellular elements of the blood and the hæmoglobin to approach their normal ratios, and especially for the number of erythrocytes, lymphocytes, and large mononuclears to be augmented, and for the hæmoglobin percentage to be increased.

The most immediate and noticeable effect of treatment was relief of dry, ineffectual cough. In all cases it was relieved, and in many patients it was limited to a necessary pulmonary toilet or disappeared entirely. This seemed to be due to the effect upon the sputum, which was increased in amount and rendered more liquid, so that it was raised with much less difficulty. This effect seemed to be attributable to the action of the pinene on the bronchial mucous membrane. In all cases the complicating bronchitis was diminished or disappeared entirely. While it is recognized that it is not always a trustworthy or permanent indication of improvement, there was noted a marked diminution of tubercle bacilli and the secondary organisms in the sputum, and in some instances they were absent in several successive examinations, when treatment had been of any duration or continuity.

The temperature, pulse, and respiration of those patients who presented any hope of improvement were reduced and steadied, the curves showing decidedly less variation. In no instance was an ac-

CHART I.


CASE NO.
NUMBER OF RED CELLS PER CUBIC MM.
Days 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230 240 Days
I
II
III
IV
V
VI
VII
VIII
OXY-PINENE TREATMENT IN N.Y. CITY
MOUNTAIN SANITARIUM WITHOUT OXY-PINENE
MOUNTAIN SANITARIUM WITH OXY-PINENE
COUNTRY SANITARIUM WITHOUT OXY-PINENE
COUNTRY SANITARIUM WITH OXY-PINENE
RESULT; ARREST
RESULT; MUCH IMPROVEMENT
IMPROVING AT OTISVILLE
AT HOME IN N.Y. CITY WITHOUT OXY-PINENE
RESULT; CONDITION ARREST OR APPROACHING ARREST
BACILLI ABSENT
RESULT; ARREST
RESULT; CONDITION APPROACHING ARREST
T.B. REDUCED IN NO. SECONDARY ORGANISM DISAPPEARED
RESULT; MUCH IMPROVED
CONTINUOUS
INTERMITTENT TREATMENT
RESULT; MUCH IMPROVED AND IMPROVING
HOME TREATMENT N.Y. CITY
RESULT; MUCH IMPROVED AND IMPROVING
Days

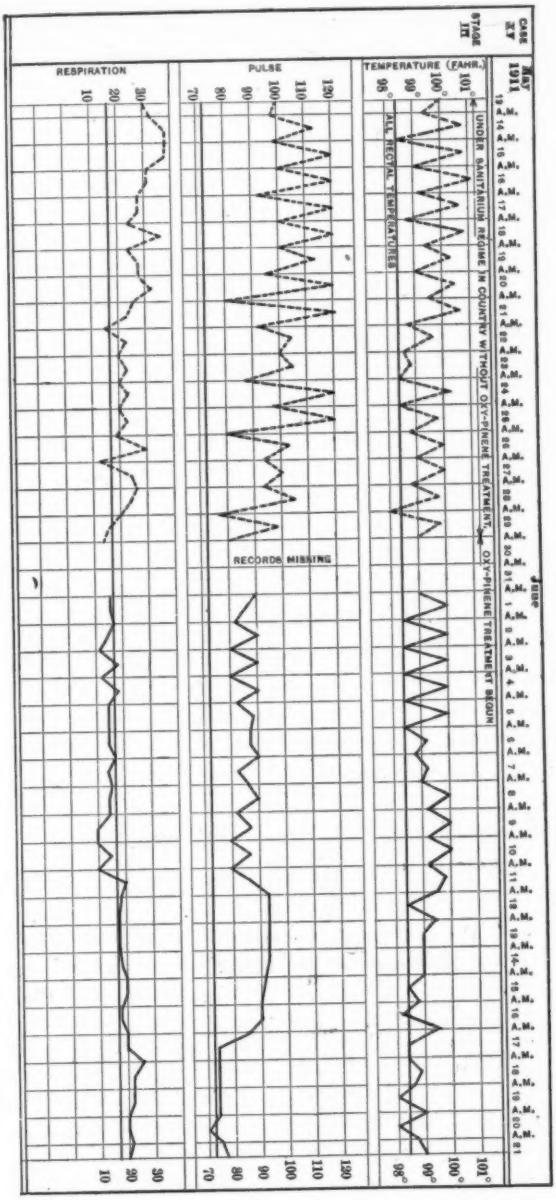

CASE XV
STAGE III
MAY 1911
TEMPERATURE (FAHR.)
PULSE
RESPIRATION
UNDER SANITARIUM REGIME IN COUNTRY WITHOUT OXY-PINENE TREATMENT
OXY-PINENE TREATMENT BEGUN
ALL RECTAL TEMPERATURES
RECORDS MISSING
JUNE

CHART 2.

celeration of respiration observed which might in itself account for improvement through better aëration of the lungs (Chart 2).

In those patients who improved there was a noticeable diminution of toxæmia, indicated by the less frequent occurrence or disappearance of rigors and hyperidrosis.

The amount of urine and the excretion of urea were increased.

The appetite was in no instance impaired, but rather seemed to be improved.

Partly perhaps from a psychological effect, but certainly also because of the relief of cough, sleep was more continuous, more sound, and more refreshing.

At no time, except when an inferior quality of turpentine was used, were there any evidences of irritation of either the heart, lungs, or kidneys.

The weight increased and the improvement, both of the general condition and of the pulmonary lesion, seemed to be as rapid and satisfactory as under any other form of treatment, and to compare favorably with that obtained under sanatorium care. Indeed, it is noticeable and interesting that all of the patients who were treated in the city made quite as rapid progress here as afterward in the country, and their improvement here was quite as marked as that of those who began their treatment in the country, or who were under sanatorium care there without treatment. This is true also of those patients who throughout their treatment have remained in the city. Interruption of the treatment was followed by a diminution of the erythrocytes (Chart 1).

*Conclusions.*—The researches and their results above reported, while preliminary and incomplete, seem to justify the following conclusions:

1. Oxypinene, prepared by the interaction of pinene vapor and dry ozonized air, possesses the valuable properties of refined and purified oil of turpentine (pinene) minus its undesirable irritating properties. In other words, pinene is modified by oxidation so that it is no longer as penetrating as pinene, nor as quickly absorbed, yet it is capable of producing the same beneficial therapeutic effects.

2. It has marked germicidal effect, *in vitro,* upon *M. pyogenes aureus, B. anthracis, B. typhosus, B. coli communis,* and *B. subtilis.* It also appears to be germicidal to the tubercle bacillus in sputum.

No experimental work has been done with tubercle *in situ.*

3. When inhaled it does not produce irritation of the respiratory

tract, neither does it produce frontal headache or renal irritation, thus decidedly differing from oil of turpentine or pinene.

4. It is a valuable expectorant. It acts as a mildly stimulating diuretic without renal irritation. It seems to stimulate the appetite and digestion and thus to improve nutrition.

5. Its use in the treatment of pulmonary tuberculosis has been beneficial, not so much from its limited bactericidal action upon tubercle bacilli as by its effect upon the associated organisms and its hæmatinic power.

6. In subacute and chronic affections of the respiratory system it is indicated as a mild stimulant to the mucous membranes and other tissues.

7. When brought in contact with infected surfaces it inhibits the growth of certain pathogenic micro-organisms, and, by its hyperæmic property, increases the circulation in the infected area, thus promoting the destruction of such organisms by phagocytosis.

A brief preliminary report upon this subject was made at a stated meeting of the New York County Medical Society on May 27, 1912. Since then the clinical observations noted have been confirmed by several colleagues and in my own hospital service.

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40 East Forty-first Street.

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# MODERN VIEWS ON THE CONSTITUTION OF THE ATOM.[1]

By A. S. Eve, D.Sc., Macdonald Professor of Physics, McGill University, Montreal.[2]

## Introduction.

The view that matter is composed of discrete entities, called atoms, which are indivisible, is one of great antiquity. It was, however, merely a speculative opinion, not based on experimental evidence.

At the present day we can affirm that atoms have a real existence, using the word "real" in the ordinary sense; for instance, as a bullet or stone may be considered real. Moreover, it is possible to perform a number of experiments which indicate clearly that atoms are themselves composed of smaller entities, termed electrons, and it is not difficult to obtain some conception of the number and distribution and motion of these electrons within the atom. Furthermore, radio-active elements, such as radium or thorium, consist of atoms in a state of disintegration or devolution, and it has been possible to detect *single* electrons projected from radio-active matter, and also to ascertain that a radium atom may eject the large nucleus of the smaller helium atom. These remarkable expulsions from the inner citadels of certain atoms take place independently of their physical surroundings, such as extremes of pressure and temperature. It is noteworthy, however, that the manner in which these heavy atoms such as uranium and radium are built up from their smaller constituents, remains a profound mystery.

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[1] Based on a lecture delivered at the meeting of the Section of Physics and Chemistry of The Franklin Institute held Thursday, December 3, 1914.

[2] Reprinted from *Jour. Franklin Institute*, 1915, p. 269.

When the seventh Duke of Devonshire presented the Cavendish Laboratory to the University of Cambridge, the first Professor of Experimental Physics appointed was Clerk Maxwell, the Newton of electricity.[3] In his great treatise on "Electricity and Magnetism" he made a notable prophecy; namely, that the discharge of electricity through a rarefied gas is a phenomenon of great interest and importance, and, when better understood, "will probably throw great light on the nature of electricity as well as on the nature of gases and of the medium pervading space."

When Maxwell died he was succeeded by Lord Rayleigh, who found the units of electricity uncertain to some five per cent. This matter needed prompt attention, for electrical supply was then becoming a commercial undertaking. Rayleigh, in a few years, made it possible to determine with good accuracy the volt, the ampère, and the ohm. He retired, owing to his multitudinous duties and interests, and the University of Cambridge was somewhat startled to find the great Chair of Physics conferred on a "boy" of twenty-seven, the illustrious J. J. Thomson.

It would seem that he was born to prove the accuracy of the first half of Maxwell's prophecy, for he promptly investigated electrical discharges in gases, and the timely discoveries of the cathode rays and of Röntgen rays enabled him to make two great forward steps, namely, the theory of gaseous ionization, and a clear view of the nature of electrons.

When a current is passed from metal plates through a highly-exhausted tube a stream of particles is projected from one plate (the cathode). It was known that these were readily deflected by a magnet, but Sir Joseph Thomson succeeded in deflecting them also by an electrostatic field. He thus showed that the cathode particles, or corpuscles, are exceedingly light, with a mass about one-eighteen-hundredth part of the hydrogen atom. These corpuscles are now usually termed electrons, and are the fundamental units or atoms of negative electricity. It is scarcely credible that this most primary conception can ever be dethroned from a foremost place in human knowledge.

Sir Joseph Thomson also gave us a theory of the manner in which a gas conducts electricity. If the molecules were all uncharged, then he believed that the gas would be a perfect insulator.

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[3] Maxwell himself termed Ampère the Newton of electricity.

The current of electricity in a gas is always carried by "ions," or charged molecules of gas which have gained, or lost, one or possibly more electrons. At low pressures or high temperatures the negative electricity may be conveyed by electrons instead of by negative ions; but positive electricity has never been found detached from atoms, or from the nucleus of atoms, so that the term positive electron has at present no concise meaning. Later we shall see Sir Ernest Rutherford's suggested interpretation of it.

It is necessary to write a few words about the radio-active substances, or radiants, as I find it convienent to call them.

There are about thirty-seven radiants known, and they are divided into three great families: (1) uranium-radium, (2) thorium, (3) actinium.

When any one of the atoms disintegrates it projects a fundamental part of the atom, either an alpha ray or a beta ray, with a high velocity into the surrounding space. That which remains of the old atom is a new atom of different physical and chemical properties to the parent atom from which the ejection took place.

The beta particle is an electron. The alpha particle is a helium atom stripped of two electrons. As the alpha particle slows down it picks up two electrons from some neighboring matter, and it is then an ordinary helium atom, and emits the same spectrum as helium.

Radiants may also emit gamma rays, which are closely analogous to Röntgen rays and are doubtless similar to light, consisting of ether undulations, but with wave-lengths several hundreds of times shorter than those of light.

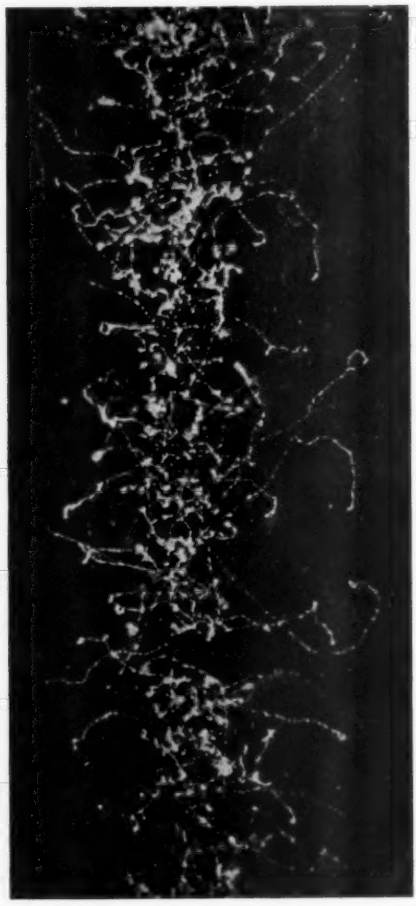
Much theoretical deduction was confirmed when C. T. R. Wilson photographed illuminated ions, mist-ladened, marking the tracks of electrons, which had been hurled forth by a pencil of Röntgen rays (Fig. 1).

As Bragg surmised, the Röntgen rays did not ionize the gas directly. They ejected high-speed electrons, and these electrons, passing through the molecules, drove some low-velocity electrons from the latter, thus giving rise to pairs of ions. The beautiful photographs of C. T. R. Wilson showed this very clearly. They bring us, moreover, abruptly face to face with one of the profound mysteries in physics.

The Röntgen rays are caused by the quick stoppage on a target of fast-moving electrons in the Röntgen tube. These rays, like light, must spread outwards with the flux of energy decreasing by the law

of inverse squares. Yet when these diverging rays strike some one out of a vast number of molecules there is ejected an electron with a speed almost equal to that of the primary cathode rays. The ejection may take place, moreover, many metres away from the tube.

FIG. 1.



No explanation of this anomaly is forthcoming. The energy cannot come from the atom, for when the *intensity* of the rays is increased there is a corresponding increase in the *number* of ejected electrons. When the *frequency* of the waves of the Röntgen rays is increased

there is an increase in the *kinetic energy* of the projected electrons. Indeed, we may write approximately that

$$\tfrac{1}{2}\, mv^2 = hn$$

where the left member is the kinetic energy of the electron, $n$ is the frequency of the X-rays, and $h$ is Planck's number equal to $6.6 \times 10^{-27}$ erg second.

This interesting relation represents a fact, but explains nothing and itself demands as much explanation as the initial difficulty.

In conversation W. H. Bragg once gave to me a striking analogy. Let the moon represent the source of X-rays, and the moonlight, shining on the earth, represent the Röntgen rays falling on a body. Just as the Röntgen rays eject here and there a high-speed electron, so the moonlight would have to cause something about the size of a pea to leap out with great velocity, first one, say, from Siberia, then one from South Africa, next from New Guinea, and so forth. Violent and very local action produced by a uniform and homogeneous radiation!

*The Counting of the Alpha Particles.*—Before C. T. R. Wilson had taken the photographs already described, Sir Ernest Rutherford had devised an apparatus which enabled him to detect the alpha particles entering, one by one, into a testing chamber in such a manner that their number could be counted. In this way he was able to deduce that the alpha particle had a charge twice as great, but opposite in sign, to the charge of an electron; that a gramme of the metal radium expelled $3.57 \times 10^{10}$ alpha particles per second, and he found accurate values for other fundamental constants.

For the detection of the individual alpha particle this eminent physicist was, with a pretty humor, justly awarded the Nobel Prize for chemistry.

*The Detection of the Individual Electron.*—The alpha-ray detector was altered and improved, and a few years later Geiger was able to report that he had succeeded in detecting *single* electrons entering a suitable orifice in his new testing chamber. As I had, owing to the kind help of the secretary, Dr. Owens, the pleasure of performing experiments with this type of apparatus at The Franklin Institute, it may be well to give a fairly full description of it.

When an electron, say a beta particle from a radiant, enters the small hole in the testing vessel $B$, it approaches a point $N$ which is almost sparking to the high-potential chamber (Fig. 2). The ions

produced by the particle, particularly the negative ions, are urged forward with a very high velocity by the intense electric field, and these ions produce more ions by collision. It is as though a temporary minute spark passed, so that the needle leaps up from zero to 36 or 40 volts. As the needle is connected to the quartz fibre *FF* this latter is at once charged, and, being between charged plates, is deflected. A stable state is swiftly re-established, owing to the high resistance *R*, and the trap is reset to show the next electron. The movements of

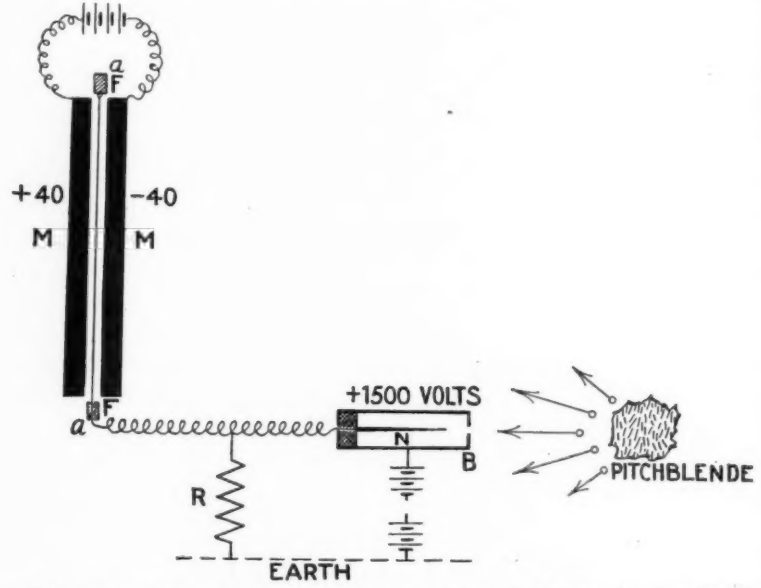



FIG. 2.—*B* is a hollow brass cylinder (4 x 1 cm.) with a small hole in the end (where the electron enters), Voltage + 1500. *N* is a fine, sharp, clean needle with its point about 8 mm. from the hole. *R* is a high resistance, about 100 megohms, of xylol and alcohol in a glass U tube. *FF* is a fine, silvered, quartz fibre between two metal plates 8 mm. apart, 15 cm. long, charged to low opposite voltages.

the quartz fibre are seen when projected on a white screen. With this apparatus many beautiful experiments can be shown, such as the range of the alpha particles from polonium; individual alpha particles passing through a pinhole in paper; the reflection of scattering of rays from lead or from aluminum, in which case the lead is the more effective; the long-distance effect of the gamma rays and their highly-penetrating nature. But the most excellent and impressive sight is that of a piece of pitchblende, just as it came from the mine in Bohemia, continually expelling alpha and beta particles into the

surrounding air. Remember also that it is capable of continuing to do so for a period exceeding one thousand million years.

*On the Nucleus of Atoms.*—Sir Joseph Thomson had suggested an atomic structure having a number of electrons revolving in concentric circles within a vague entity consisting of positive electricity. Sir Ernest Rutherford, working with Geiger, found that when alpha particles bombarded thin gold leaf the great majority of the particles passed through, but about one in every eight thousand returned on the side of entry. He came to the conclusion that the returning alpha particle had encountered a highly-charged nucleus. Working out this idea on the basis of Newtonian mechanics, he concluded that the nucleus was small in its effective dimensions, but that it had a charge equal to about one-half of the atomic weight of the atom. This idea was amply verified by a long series of experiments, and it fitted well with results obtained by Barkla, who, stimulating matter with Röntgen rays, obtained evidence that an atom contained electrons to a number about half that of the atomic weight.

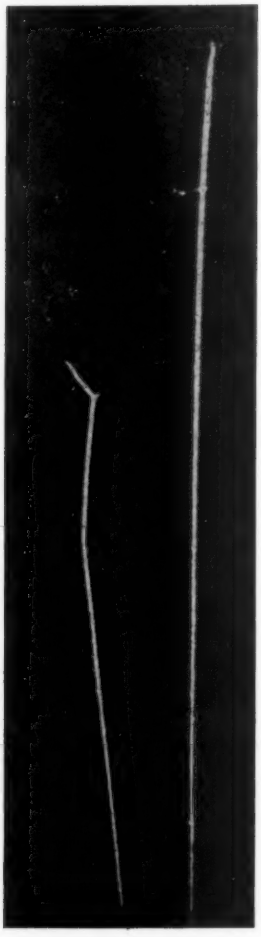
Putting these results together, we obtain something resembling a miniature solar system, with the minute central body consisting of a large positive charge, and in concentric surrounding rings are electrons revolving like planets,[4] but perhaps with several in each ring, and so adjusted that their total charge, which is negative, balances the positive charge on the nucleus.

*The Alpha Particle and Hydrogen Nucleus.*—In one of Wilson's photographs of the track of an alpha particle (Fig. 3) there appears, near the end of the path, a small projecting spur, which he explained as due to an atom of an air molecule, struck by an alpha particle, receiving sufficient velocity to ionize the air for a short distance. It immediately occurred to Rutherford that if an alpha particle passed through hydrogen, then the light hydrogen atom, or rather its nucleus, would be projected, not merely to a greater distance than the nucleus of the oxygen or nitrogen atom, but to almost four times the distance of the alpha particle itself. This forecast was verified by Marsden, using a zinc sulphide screen, when the scintillations due to the hydrogen nuclei were seen at a range nearly quadruple that of the alpha particles. This important verification has placed the theory of the nucleus on a foundation which excludes doubt as to its reality.

[4] There is, however, no direct experimental evidence that the electrons revolve. They may vibrate about stable positions.

*The Beta and Gamma Rays.*—Another photograph was obtained by Wilson showing the long range of the electron expelled by incident gamma rays. In air at atmospheric pressure this secondary beta particle will traverse more than a metre. As will be seen later, the gamma rays are electromagnetic disturbances having a minute

FIG. 3.



wave-length, even compared with light waves, and a correspondingly high frequency. The kinetic energy is, as with Röntgen rays propelling electrons, again approximately equal to $h$ times the frequency, when $h$ is Planck's constant. The mechanism by which these phe-

nomena occur is unknown, whether we consider electrons projected by ultraviolet light, Röntgen rays, or gamma rays.

*Planck's Constant.*—When in a reflecting enclosure there is a heated body and, necessarily, ether, the former has a limited number of degrees of freedom, and the latter an unlimited number. It may, therefore, be expected that, as theory appears to indicate, the energy of the body would decrease and that of the ether increase, particularly towards vibrations of the shorter wave-lengths. Experiment proves that this does not occur, and that the distribution of energy is utterly different from that which Newtonian mechanics demand. Planck found himself able to explain this distribution only on the supposition that energy could leave the oscillators in the body by exact *quanta*, the magnitude of which was in each case proportional to the frequency of the oscillator, or equal to $h\nu$. Shortly before his death Poincaré thoroughly investigated this hypothesis and concluded that an explanation on the basis of Planck's hypothesis was inevitable, and that no other view was in accordance with observed radiation phenomena. An able summary of the whole subject has been given by Jeans in a report published by the Physical Society of London.[5] We have, therefore, a unique situation in physics. The quantity $h$ has been introduced and its magnitude determined without our having any approximate idea of what $h$ represents. To the student of radio-activity it is the ratio of the number of units of the kinetic energy of the projected electron, divided by the frequency of the incident, electromagnetic disturbance, or possibly by some exact multiple of that frequency.

*Röntgen Rays and Crystal Reflection.*—It was foreseen by Laue, at a time when the potentialities of Röntgen rays appeared almost exhausted, that these rays would be scattered in a definite direction from any set of orderly parallel planes in which the atoms of a crystal are arranged. An analogy may be useful. If troops with fixed bayonets are not drawn up in rank the sunlight reflected from the bayonets will give to a spectator a glint here and there. In well-dressed ranks, however, a spectator will in some positions see no reflections, but in other positions, when the angles of reflection and incidence are equal, he will obtain a powerful flash from all the bayonets in all the ranks.

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[5] "Report on Radiation and the Quantum Theory," by J. H. Jeans, *The Electrician* Printing Company, Fleet Street, London.

Professor W. H. Bragg and his son have developed this method and obtained information as to the distribution of atoms in various crystals, the distance between the atoms, and the wave-lengths of the Röntgen rays. He has himself summarized this work in an article published recently in *Science* (December 4, 1914).

*Crystal Reflection of Gamma Rays.*—The gamma rays have been reflected from the regular layers of atoms in a crystal in a manner quite similar to that employed with Röntgen rays, a radiant taking the place of the X-ray tube. In this way Rutherford has found that the wave-lengths of the most penetrating gamma rays, glancing from the crystal face at 42′, is about $0.7 \times 10^{-9}$ cm. This is the smallest wave-length known, but the phenomenon may as justly be attributed to an electromagnetic disturbance in the ether as a radiotelegraph wave with a length of several kilometres.

It is interesting to note, in some papers of Rutherford's, how he appears to use language and ideas which are at present totally irreconcilable. I am not venturing to criticise this, for the statements do indeed represent the facts. At one time Rutherford is speaking of "a gamma ray," thus suggesting *linear* propagation of energy, and at another time he is discussing the wave-length of a gamma ray with a meaning applicable to ordinary light radiation and therefore involving an expanding wave front. We are reminded of Newton's troubles in explaining diffraction by a corpuscular theory, and concluding that light has an "eel-like" motion.

*Atomic Number.*—Since the positive charge on the nucleus of an atom is about half the atomic weight, and since that charge is necessarily a whole number when expressed as a multiple of the magnitude of the charge of an electron, it has been suggested by van den Broek that there is a fundamental and important number connected with every element, known as the atomic number. This number is possibly the place of the element in the periodic table (H 1, He 2, Li 3, Be 4, Bo 5, C 6, etc.). This theory has had strong confirmation from a series of experiments by Moseley. He exposed most of the elements to the bombardment of electrons in a vacuum tube, these elements forming, in turn, the anticathodes of a Röntgen tube. The natural or characteristic radiations of the elements were reflected from a crystal surface, and the frequencies of the vibrations were thus determined. After a correction for the outer electrons, it was found that in every case the frequency was proportional to the square of an integer which was identified with the atomic number. Accord-

ing to Sir Joseph Thomson, when an atom has, suppose, three rings of revolving electrons, the outer ring is that influenced by ionization and is investigated by spectrum analysis, the inner ring is connected with the penetrating, or hard, or K series of characteristic Röntgen radiations, and the middle ring with the less penetrating, or soft, or L series. To the nucleus we must look for the main effects of mass and inertia, and gravitational attraction, and, when they exist, for the radio-active transformations and expulsions.

*Bohr's Theories.*—It has been pointed out that when a single electron revolves round a unit charge nucleus, as in the case of hydrogen, that by electromagnetic theory there should be a continued stream of energy radiated away into space, necessarily demanding that the revolving electron would lose speed and fall into the nucleus. To overcome this and similar difficulties, Bohr has suggested a theory of stable states, non-radiating, with the angular momentum an exact multiple of $h/2\pi$, where $h$ is Planck's constant. When the multiple is, for reasons unknown, diminished by unity, the electron abruptly changes from the old stable state to the next stable position, and in doing so radiates away an exact quantum such as Planck first conceived. It must be admitted that these ideas appear at first highly imaginative, and they might well be ignored but for the remarkable degree of success which they have already achieved. Notably he foretold the existence of certain lines in the ultra-violet spectrum of hydrogen, and these were subsequently discovered by Lyman. He identified lines found by Paschen in the infra-red, and also obtained an excellent numerical verification between his theory and the value of the constant of Rydberg which links up the spectral series of various elements. Perhaps the most interesting suggestion is that lines seen in the spectrum of certain stars may be assigned to hydrogen in a state of extreme tenuity, so that the electron revolves in a greatly-enlarged orbit about the nucleus, a state which it is impossible to imitate in the small vessels of our laboratories.

*Valency Law of Radiants.*—A band of chemists who have made a careful study of the properties of the radio-elements have succeeded in the discovery of an interesting law which removes the difficulty of finding places in the periodic table for all the radiants, about thirty-seven in number. A full account of this work is given by Soddy in "The Chemistry of the Radio-elements" (Longmans, Green & Co., 1914).

Briefly, it has been found that when a radiant expels an alpha

particle, thus reducing the charge on the nucleus by two electronic units, there is a corresponding change of valency, say from tetravalent to divalent, so that the new product is two columns to the left in the periodic table, while the decrease of atomic weight is four. When a beta particle is expelled there is no effective change of atomic weight, but the nucleus charge or atomic number has increased by one, since the loss of a negative is equivalent to the gain of a positive electronic unit charge. The subsequent product is now found one column to the right in the table, relative to the parent element. Two elements with different atomic weight, but with the same nucleus charge, may find themselves in the same place in the periodic table, and are known as isotopes. Such elements have chemical and physical properties so similar that they are at present deemed inseparables or non-separables. As an example, it is possible to obtain radium D as it forms from the disintegration of radium C. If this radium D is mixed with lead, separation becomes impossible, because their chemical properties are identical. This theory has already achieved a notable success. In the early days of radioactivity Sir William Crookes obtained uranium X by chemical separation from uranium, and it was shown that it was a linear descendant. The uranium was found to eject two sets of alpha particles of different ranges, so that it was presumably two radiants and not one. The law above described suggested both the presence of an undiscovered radiant and also its chemical properties. This substance, uranium X2, or brevium, for it is short-lived, was quickly discovered.

The conclusion arrived at is set forth in the following typical scheme, where uranium 1 and uranium 2 are inseparables or isotopes, with atomic weights differing by 4, but with atomic numbers and valencies identical.

| IV. | V. | VI. | At. wts. |
|---|---|---|---|
| Ur X1 → $\beta$, 90 | Ur X2 → $\beta$, 91 | Ur 2 $a$, 92 | 234.5 |
| | | Ur 1 $a$, 92 | 238.5 |

*The Positive Electron.*—In the early days of the electron theory it was not unnaturally supposed that the positive electron was similar in general character to the negative electron, the two, of course, neutralizing one another. The diligent search of many eminent physicists has failed to obtain evidence of any such entity, and in no case has a positive electronic charge been observed except accompanied with a mass of atomic dimensions. Sir Joseph Thomson has found that the hydrogen atom, alone of the elementary atoms, never loses more than one electron. It has been suggested by Sir Ernest Rutherford that the long-sought positive electron may, in fact, be the nucleus of the hydrogen atom, and, in that case, that its mass would be 1800 times as great as the mass of the negative electron. If this mass is electromagnetic in character, it must vary inversely as the radius, so that the positive electron would have a sphere of action extremely minute, even compared with the negative electron. The radii of the three spheres would then be of the following orders:

Atom, $10^{-8}$ cm.
Electron, $10^{-13}$ cm.
Positive electron, $10^{-16}$ cm.

It is clear that the investigation of the inner constitution of the electrons will offer formidable difficulties to future generations of physicists.

## Conclusion.

There are generally not a few men of small intellect or foresight who ask, "What is the good of these philosophical discoveries?" Such is not the attitude of those who are engaged in the practical work of applying scientific discoveries to the benefit of mankind. But, apart from inventions, so often misdirected to the destruction rather than the elevation of the human race, it is well to urge continually the high aim of the search for truth for its own sake, wheresoever it may lead us. It may be noted that the discoveries set forth in this brief summary have been achieved by savants in the western half of Europe, and it may be asked if the education in the New World is at the present time sufficiently thorough, imaginative, and philosophical. In any case, the future improvement of mankind is likely to arise from education in the sense of development of knowledge, character, and principles, rather than from the acquisition of wealth, or by the multiplication of material resources.

# CURRENT LITERATURE.

## Alkaloidal Content of Stramonium Leaves.

In Bulletin 692 of the University of Wisconsin, H. A. Langenhan records the results of some investigations undertaken to determine the alkaloidal content of several species of stramonium that have been examined chemically, and to ascertain the alkaloids present in the leaf of a given species for a succession of years. The results of the assay of *Datura Stramonium Gigantea* and *Datura Stramonium Inermis* bring forth the statement from the author that no satisfactory generalizations can be made. The material worked with was cultivated in the Northern Experiment Station at Madison, a co-operative experiment for the cultivation of medicinal plants by the United States Department of Agriculture and The University of Wisconsin. J. K. T.

## Wisconsin Wormwood Oil.

E. R. Miller (Bulletin of the University of Wisconsin, No. 693) has made an interesting study of the chemical and physical properties of this oil. As the wormwood industry is the oldest medicinal plant industry in the State, the oil having been produced for over fifty years, it seemed that an investigation having for its object a more systematic cultivation and distillation of the plant would be welcome to those engaged in this industry. Work of this kind, if consistently kept up, will eventually be of material aid and help to make Wisconsin oil the best in the market. J. K. T.

## Oils of Eupatorium.

E. R. Miller (Bulletin of the University of Wisconsin, No. 693) has made an exhaustive chemical study of the oils of several species of *Eupatorium*. A tabulation gives the time of collection, the yield of oil, the specific gravity, index of refraction, rotation in a 100-mm. tube, percentage of methoxy group, saponification number, saponification number after acetylating, the acid number, and the percentage of thymohydroquinone dimethyl ether calculated from the percentage of methoxyl. J. K. T.